IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015-GBW
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA Counterclaimants, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Counterclaim Defendants.	

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MEMORANDUM OPINION

July 3, 2023
Wilmington, Delaware

GREGORY B. WILLIAMS
UNITED STATES DISTRICT JUDGE

Plaintiff/Counter-Defendant Nippon Shinyaku Co. Ltd. and Counter-Defendant NS Pharma, Inc. (collectively "NS") alleges that Defendant/Counter-Plaintiff Sarepta Therapeutics, Inc. ("Sarepta") infringes U.S. Patent Nos. 9,708,361 ("the '361 patent"); 10,385,092 ("the '092 patent"); 10,407,461 ("the '461 patent"); 10,487,106 ("the '106 patent"); 10,647,741 ("the '741 patent); 10,662,217 ("the '217 patent"); and 10,683,322 ("the '322 patent") (collectively, the "NS Patents"). D.I. 86. The NS Patents generally relate to a morpholino antisense oligomer that induces skipping of exon 53 of the human dystrophin gene to treat Duchenne Muscular Dystrophy ("DMD"). In response, Sarepta and Counter-Plaintiff The University of Western Australia ("UWA") assert counterclaims for infringement of U.S. Patent Nos. 9,994,851 ("the '851 patent"), 10,227,590 ("the '590 patent"), and 10,266,827 ("the '827 patent") (collectively, "the Wilton Patents") against NS. D.I. 195. The Wilton Patents generally relate to treatments for DMD using an antisense oligonucleotide with bases that are complementary to those of its target region, which induce skipping of that target exon when the pre-mRNA is further processed to produce dystrophin protein.

Before the Court is the issue of claim construction of multiple terms across the NS Patents and the Wilton Patents. The Court has considered the parties' joint claim construction briefs and the accompanying appendices. D.I. 166; D.I. 167; D.I. 168; D.I. 169; D.I. 170; D.I. 171; D.I. 173; D.I. 174. The Court held a *Markman* hearing on May 3, 2023 (the "*Markman*," Tr. __).[1]

[1] The Court writes for the benefit of the parties and assumes their familiarity with this action.

I. LEGAL STANDARDS

"It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (internal quotation marks omitted); *see also Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989) ("A claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention"). "[T]here is no magic formula or catechism for conducting claim construction." *Phillips*, 415 F.3d at 1324. The Court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.* The ultimate question of the proper construction of a patent is a question of law, although subsidiary fact-finding is sometimes necessary. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (quoting *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996)).

"The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." *Thorner v. Sony Comput. Ent. Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012) (citing *Phillips*, 415 F.3d at 1312–13). A person of ordinary skill in the art "is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313.

"When construing claim terms, the court first looks to, and primarily rel[ies] on, the intrinsic evidence, including the claims themselves, the specification, and the prosecution history of the patent, which is usually dispositive." *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1276 (Fed. Cir. 2013). "Other claims of the patent in question, both asserted and

unasserted, can . . . be valuable" in discerning the meaning of a disputed claim term because "claim terms are normally used consistently throughout the patent," and so, "the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Phillips*, 415 F.3d at 1314. In addition, "[d]ifferences among claims can also be a useful guide[.]" *Id.* For example, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15.

In addition to the claim, the Court should analyze the specification, which "is always highly relevant to the claim construction analysis ... [as] it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. "Even when the specification describes only a single embodiment, [however,] the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)). And, the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004).

The Court "should also consider the patent's prosecution history, if it is in evidence." *Markman*, 52 F.3d at 980. The prosecution history "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution[.]" *Phillips*, 415 F.3d at 1317.

In some cases, the Court "will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. Overall, while extrinsic evidence may be useful, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Phillips*, 415 F.3d at 1317 (internal quotation marks and citations omitted).

II. DISPUTED TERMS – THE WILTON PATENTS

A. "antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA"

At the outset, the parties dispute whether the phrase "antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA" (the "Antisense Oligonucleotide Phrase") should be construed in its entirety rather than only the terms of the Antisense Oligonucleotide Phrase that are in dispute. D.I. 166 at 8-10, 13-14. Sarepta contends that the Antisense Oligonucleotide Phrase should be construed as a whole rather than evaluating terms in isolation because "claim language must be construed in the context of the claim in which it appears" since "[e]xtracting a single word from a claim divorced from the surrounding limitations can lead construction astray." D.I. 166 at 10 (quoting *IGT v. Bally Gaming Int'l, Inc.*, 659 F.3d 1109, 1117 (Fed. Cir. 2011)). NS disagrees, arguing that Sarepta's proposal is "legally erroneous" because, while the Court must resolve "actual dispute[s] regarding the proper scope of . . . claims," it "[is] not (and should not be) required to construe every limitation present in a patent's asserted claims."

D.I. 166 at 13-14 (quoting *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F. 3d 1351, 1362 (Fed. Cir. 2008)). In other words, by construing the entire Antisense Oligonucleotide Phrase rather than just those terms in dispute, NS contends that Sarepta omits key limitations of the phrase and "deprive[s] the disputed terms of their original context." *Id.* at 14.

The Court agrees with NS that only those terms actually in dispute require a construction. Although Sarepta is correct that "the context of the surrounding words of the claim . . . must be considered in determining the ordinary and customary meaning of those terms," *see ACTV, Inc. v. Walt Disney Co.*, 346 F.3d 1082, 1088 (Fed. Cir. 2003), the Federal Circuit mandates that "only those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy," *see Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999). *See U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997) ("Claim construction is a matter of resolution of disputed meanings and technical scope, to clarify and when necessary to explain what the patentee covered by the claims, for use in the determination of infringement."). The parties agree that the scope of the entirety of the Antisense Oligonucleotide Phrase is not in dispute. Accordingly, because only particular terms of the Antisense Oligonucleotide Phrase are in dispute, the Court will only construe those disputed terms rather than the phrase as a whole.

B. "a base sequence"

The claim term "a base sequence" appears in claims 1 and 2 of the '851 patent, claims 1 and 2 of the '590 patent, and claim 1 of the '827 patent. The parties' competing proposed constructions for "a base sequence" are set out in the chart below:

Claim Term	Sarepta's Construction	NS's Construction
"a base sequence"	No construction needed. **Alternatively**: plain and ordinary meaning, which means "a linear sequence of bases"	"any sequence of bases that is part of the antisense oligonucleotide"

The crux of the parties' dispute is whether "a base sequence" can be a portion of the claimed oligonucleotide, or whether it must include all bases of the "antisense oligonucleotide," i.e., each antisense oligonucleotide has a single base sequence. Sarepta contends that no construction is necessary because a person of ordinary skill in the art would understand, based on the plain language of the claims, that "a base sequence" includes all of the bases in the antisense oligonucleotide. D.I. 166 at 30. However, if the Court were inclined to construe the disputed term, Sarepta argues that, when viewed in context of the Wilton Patents' intrinsic record, "a base sequence" has a plain and ordinary meaning of "a linear sequence of bases." *Id.* at 31-32. NS disagrees, arguing that the Wilton Patents' use of the word "comprising" prior to reciting the disputed term indicates that "a base sequence" must be at least a portion of the claimed antisense oligonucleotide, but it need not be the entirety of the antisense oligonucleotide. *Id.* at 18-19.

"It is axiomatic that we will not narrow a claim term beyond its plain and ordinary meaning unless there is support for the limitation in the words of the claim, the specification, or the prosecution history." *3M Innovative Props. Co. v. Tredegar Corp.*, 725 F.3d 1315, 1333 (Fed. Cir. 2013) (citations omitted). "If the intrinsic record supports several definitions of a term, the term may be construed to encompass all such consistent meanings." *Wasica Fin. GmbH v. Cont'l Auto. Sys., Inc.*, 853 F.3d 1272, 1281 (Fed. Cir. 2017) (citation omitted). "Therefore, absent a clear disavowal or alternative lexicography by a patentee, he or she 'is free to choose a broad term

and expect to obtain the full scope of its plain and ordinary meaning.'" *Id.* at 1282 (quoting *Thorner*, 669 F.3d at 1367).

The Court begins its analysis with the language of the claim itself. Use of the disputed term in claim 1 of the '851 patent is instructive:

> 1. An antisense oligonucleotide of 20 to 31 bases comprising ***a base sequence*** that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69), wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), in which uracil bases are thymine bases, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping; or a pharmaceutically acceptable salt thereof.

See '851 patent at claim 1 (emphasis added).

The plain language of the claim suggests, as does NS, that the claimed antisense oligonucleotide includes "a base sequence" that meets the subsequently recited limitations, i.e., "is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA" and "comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195)." *See* '851 patent at claim 1; *see also* '590 patent at claim 1; '827 patent at claim 1. As NS indicates, the claim language uses the word "comprising," "which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." *Vectura Ltd. v. Glaxosmithkline LLC*, C.A. No. 16-638-RGA, 2018 WL 4700222, at *4 (D. Del. Oct. 1, 2018) (quoting *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997)). Thus, absent a teaching or disclaimer to the contrary, the claim language does not require that the claimed antisense oligonucleotide consists only of the recited "base sequence" while excluding other bases, as Sarepta asserts. D.I. 166 at 30-31. Rather,

the plain language only requires that the claimed antisense oligonucleotide includes at least "a base sequence," while allowing for additional elements, e.g., additional bases.

Additionally, and contrary to Sarepta's position, NS's proposed construction does not use the recited term "comprising" as a pretext to "wrongly eliminate[] the requirement for 100% complementarity by expanding the claims to cover multiple 'base sequences,' including non-complementary base sequences." D.I. 166 at 31 (citations omitted). Indeed, the claim also recites "a" base sequence. *See* '851 patent at claim 1; *see also* '590 patent at claim 1; '827 patent at claim 1. Notably, the Federal Circuit "has repeatedly emphasized that an indefinite article 'a' or 'an' in patent parlance carries the meaning of 'one or more' in open-ended claims containing the transitional phrase 'comprising.'" *United Therapeutics Corp. v. Liquidia Techs., Inc.*, 2022 WL 3910252, at *16 (D. Del. Aug. 31, 2022) (quoting *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000)). There is no language in the claims or specification that necessitates a departure from this general rule. *See Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342-43 (Fed. Cir. 2008) ("An exception to the general rule that 'a' or 'an' means more than one only arises where the language of the claims themselves, the specification, or the prosecution history necessitate a departure from the rule."). Accordingly, the claims' plain language does not support Sarepta's argument that "[a] skilled artisan would understand that the 'base sequence' includes all of the bases in the antisense oligonucleotide[,]" and excludes all other bases. D.I. 166 at 19. Rather, a person of ordinary skill in the art would understand that the claimed antisense oligonucleotide includes "a base sequence" meeting the subsequently recited claim limitations, e.g., length, complementarity, and may even include more than one base sequence.

Furthermore, Sarepta's proposed construction is incorrect because it would improperly render the claim language "comprising a base sequence" superfluous. Sarepta contends that the

intrinsic record supports that "the entire linear sequence of bases in an antisense oligonucleotide forms a base sequence, i.e., the overall length of an antisense oligonucleotide is the same as the length of the base sequence itself." *See* D.I. 171, Ex. 37 ¶ 51. However, if Sarepta's position was correct, then the claim would read as if the language "comprising a base sequence" were deleted. *See Wasica Fin. GmbH v. Cont'l Auto. Sys., Inc.*, 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017) ("It is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous."). In other words, the term "comprising" affirms that the claimed "a base sequence" need not, although it may, span the entirety of the antisense oligonucleotide. *Genentech*, 112 F.3d at 501. More so, Sarepta improperly conflates the claims' requirement for "a base sequence"—that it be "100% complementary to consecutive bases in a target region"—to the entire "antisense oligonucleotide." Indeed, the patentee chose to recite "a base sequence" as a separate claim term from "antisense oligonucleotide," which suggests that the two terms have distinct meanings. *See Bd. of Regents of the Univ. of Texas Sys. v. BENQ Am. Corp.*, 533 F.3d 1362, 1371 (Fed. Cir. 2008) ("Different claim terms are presumed to have different meanings."). Finally, Sarepta's proposed construction improperly relies on certain embodiments found in Table 1A of the Wilton Patents to limit the term to only a sequence of bases that are ***linear***, *see* D.I. 166 at 31-32 (citing '851 patent at cols. 7-19), even though these embodiments are narrower than the scope dictated by the more general language of the claims. *KCJ Corp.*, 223 F.3d at 1356 ("[P]articular embodiments appearing in a specification will not be read into the claims when the claim language is broader than such embodiments."); *see also SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1340 (Fed. Cir. 2001).

Therefore, the plain language of the claims supports that "a base sequence" need only be included in the claimed antisense oligonucleotide and that it need not, although it may, span the

entirety of the antisense oligonucleotide. The intrinsic record also supports that the claimed antisense oligonucleotide may include more than a single sequence of bases that is 100% complementary to one consecutive segment of pre-mRNA. For example, the Wilton Patents' specifications disclose "weasel" embodiments of antisense oligonucleotides, which are "cunningly designed antisense oligonucleotide" formed "by joining together two or more antisense oligonucleotide molecules." *E.g.*, '851 patent at 4:56-62; *see SynQor, Inc. v. Artesyn Techs., Inc.*, 709 F.3d 1365, 1378-79 (Fed. Cir. 2013) ("A claim construction that 'excludes the preferred embodiment is rarely, if ever, correct and would require highly persuasive evidentiary support.") (quoting *Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1290 (Fed. Cir. 2010)). The applicants' exchange with the Patent Office also supports this construction. *Phillips*, 415 F.3d at 1317 ("[T]he prosecution history provides evidence of how the PTO and the inventor understood the patent."). During prosecution of the '851 patent, the applicant acknowledged that the claimed antisense oligonucleotide may contain a "sequence" of bases that does not span the entirety of the oligonucleotide. *See* D.I. 169, Ex. 22 at SRPT-VYDS-0004785 (In response to an obviousness rejection, Applicant explained that "[t]he Office . . . selects SEQ ID NO: 29 (h53AON1), which [the Office] contends is a 18-mer oligonucleotide ***having a sequence identical to three nucleotides*** of SEQ ID NO: 195") (emphasis added). That a "sequence" of bases need not span the entirety of the oligonucleotide is further confirmed by the Examiner's argument that a person skilled in the art would "try and enhance the oligonucleotide by . . . a common and efficient strategy [of] . . . synthesiz[ing] and test[ing] longer oligonucleotides ***containing within them the sequence*** known to have the desired activity." *See id.* at SRPT-VYDS-0004611 (emphasis added).

Finding no evidence in the claims, specification, or prosecution history to support limiting "a base sequence" to the entirety of the claimed antisense oligonucleotide, the Court will apply the plain and ordinary meaning, which is the default in claim construction. *Phillips*, 415 F.3d at 1316. Accordingly, the Court will construes the term "a base sequence" to have its plain and ordinary meaning, which means "any sequence of bases that is part of the antisense oligonucleotide."

C. "a target region"

The claim term "a target region" appears in claims 1 and 2 of the '851 patent, claims 1 and 2 of the '590 patent, and claim 1 of the '827 patent. The parties' competing proposed constructions for "a target region" are set out in the chart below:

Claim Term	Sarepta's Construction	NS's Construction
"a target region"	Not indefinite. **Alternatively**: plain and ordinary meaning, which means "a segment of the pre-mRNA"	Indefinite

The crux of the parties' dispute is whether the term "a target region" is indefinite or, whether a person of ordinary skill in the art would understand, with reasonable certainty, its meaning based on the Wilton Patents' intrinsic record. NS contends that "a target region" is indefinite because "a [person of ordinary skill in the art] would not be reasonably certain regarding what portion(s) of the pre-mRNA must be 'targeted' to satisfy this claim language." D.I. 166 at 24 (quoting D.I. 171, Ex. 43 ¶ 53). Indeed, NS argues that the Wilton Patents' specifications confirm that "a target region" is indefinite because they refer to "targeting" a portion of pre-mRNA in at least three distinct ways. *Id.* at 24-25. Sarepta disagrees, arguing that, based on the intrinsic record, the term is readily understood with reasonably certainty to mean "a segment of pre-mRNA"

to which the claimed antisense oligonucleotide is intended to bind. D.I. 166 at 33 (citing D.I. 171, Ex. 37 ¶¶ 63-64; *id.*, Ex. 53 ¶23).

Section 112 of the Patent Act requires that the claims of a patent "particularly point[] out and distinctly claim[] the subject matter which the inventor . . . regards as the invention." 35 U.S.C. § 112(b). The "primary purpose of the definiteness requirement" contained in § 112(b) "is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, *e.g.*, competitors of the patent owner, can determine whether or not they infringe." *All Dental Prodx, LLC v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002).

"A patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014). To determine indefiniteness, courts examine "the patent record—the claims, specification, and prosecution history—to ascertain if they convey to one of skill in the art with reasonable certainty the scope of the invention claimed." *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1341 (Fed. Cir. 2015). While a "'potential infringer'" need not "be able to determine ex ante if a particular act infringes the claims," the patentee must "apprise the public 'of what is still open to them[]'" such that "a person of ordinary skill in the art could determine whether or not an accused product or method infringes the claim." *Niazi Licensing Corp. v. St. Jude Med. S.C., Inc.*, 30 F.4th 1339, 1346-47 (Fed. Cir. 2022) (citations omitted) (internal quotations omitted). The challenger must "prov[e] indefiniteness by clear and convincing evidence." *BASF Corp. v. Johnson Matthey Inc.*, 875 F.3d 1360, 1365 (Fed. Cir. 2017).

Like claim construction, definiteness is a question of law, but the Court must sometimes render factual findings based on extrinsic evidence to resolve the issue of definiteness. *See Sonix Tech. Co. v. Publications Int'l, Ltd.*, 844 F.3d 1370, 1376 (Fed. Cir. 2017). "[A]ny fact critical to a holding on indefiniteness must be proven by the challenger by clear and convincing evidence." *One-E-Way, Inc. v. Int'l Trade Comm'n*, 859 F.3d 1059, 1062 (Fed. Cir. 2017) (cleaned up).

NS has not carried its burden of demonstrating, by clear and convincing evidence, that the disputed term "a target region" is indefinite. NS contends that, based on the intrinsic record, "a target region" is susceptible to three different meanings that produce materially different claim scopes, thereby failing to inform a person of ordinary skill in the art as to the scope of the claims. D.I. 166 at 26. However, when viewed in light of the Wilton Patents' intrinsic record, a person of ordinary skill in the art would reject NS's first and second proffered interpretations of "a target region" and, instead, understand, with reasonable certainty, that the disputed term means "a segment of the pre-mRNA." *See Nevro Corp. v. Bos. Sci. Corp.*, 955 F.3d 35, 41 (Fed. Cir. 2020) (indefiniteness is not established by showing that a claim is "susceptible to different interpretations" because "[s]uch a test would render nearly every claim term indefinite so long as a party could manufacture a plausible construction").

First, NS argues that the Wilton Patents' specifications use the word "target" to refer to less than the entire pre-mRNA of the exon of interest—namely, "to refer to the particular motifs or regulatory regions on a pre-mRNA transcript being targeted (e.g., acceptor site, donor site, enhancers, silencers)." D.I. 166 at 25 (citing D.I. 171, Ex. 43 ¶¶ 54-57 (describing exemplary disclosures)). In other words, the '851 patent's specification purportedly identifies regulatory regions as "preferred target site(s)" and "[t]he most obvious or readily defined targets for splicing intervention." *See* '851 patent at 3:22-29, 4:30-38, 25:12-17; *see also id.* at 3:67-4:3 (discussing

prior work of "targeting the acceptor region of the mouse dystrophin pre-mRNA"); *id.* at 23:24-28 (describing "antisense molecule(s) . . . targeted to nucleotide sequences involved in splicing"). However, a person of ordinary skill in the art, reading the entirety of the Wilton Patents' intrinsic record, would not consider this to be a plausible interpretation because the plain claim language is silent as to any particular motif or regulatory region. In fact, the claims define the target region positionally as a segment of exon 53 and have additional limitations that require at least 12 consecutive bases of SEQ ID NO: 195, i.e., nucleotides +23+47 of exon 53, and 100% complementarity. *See, e.g.*, '851 patent at claims 1, 2; '590 patent at claims 1, 2; '827 patent at claim 1. As such, based on the plain claim language of the Wilton Patents, a person of ordinary skill in the art would not consider "a target region" to refer to the particular motifs or regulatory regions of a pre-mRNA.

Second, NS argues that the disputed term is indefinite because a person of ordinary skill in the art would also recognize that the specifications of the Wilton Patents repeatedly use the word "target" to broadly identify an exon of interest. *See* D.I. 166 at 26 (citing '851 patent at 23:62-24:3 (referencing "some targets such as exon 19," and "some other targets, such as murine dystrophin exon 23"); *id.* at 24:21-25 (noting that "[i]n other exons targeted for removal, masking the donor splice site did not induce any exon skipping"); *id.* at 23:31-35). While the specifications of the Wilton Patents do reference "an exon of interest" when using the term "target," a person of ordinary skill in the art would also not consider this to be a reasonable interpretation of the disputed term because the claims themselves already identify exon 53 as the exon of interest.

Third, NS contends, and Sarepta agrees, that the Wilton Patents' specification also uses "target" to refer more narrowly to "the exact bases of pre-mRNA to which an antisense oligonucleotide anneals (or binds)." *See* D.I. 166 at 25 (citing D.I. 171, Ex. 43 ¶¶ 54, 58).

However, NS asserts that Sarepta unilaterally adopts this interpretation as the plain and ordinary meaning of "a target region" while simultaneously "failing to recognize that the specification only uses the exact language 'target region' twice, and that neither of those usages apply the annealing site meaning." *Id.* at 26. But NS's argument ignores that the specification's first use of the disputed term is as a verb, i.e., "to target" regions of pre-mRNA, rather than as a noun as recited in the claims. *Compare* '851 patent at 4:32-35 ("Simply designing antisense molecules ***to target*** regions of pre-mRNA presumed to be involved in splicing is no guarantee of inducing efficient and specific exon skipping."), *with id.* at claim 1 ("An antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of ***a target region*** of exon 53 of the human dystrophin pre-mRNA . . ."); *see also Charles Smith Enterprises, LLC v. Catapult Sports, Inc.*, C.A. No. 21-1278-CFC, D.I. 62 at 2 (D. Del. Feb. 8, 2023) ("Nouns should not be construed as anything other than nouns . . ."). More importantly, NS's reliance on the specification's second use of the disputed term belies its own argument that a person of ordinary skill in the art would not consider this interpretation to be the plain and ordinary meaning of "a target region." That is, the specification explains the common usage of antisense molecule nomenclature, which identifies the target region of the particular exon through annealing coordinates. *See* '851 patent at 22:44-55; *see also* D.I. 171, Ex. 53 ¶ 74. Neither party disputes that the specification also consistently refers to "annealing sites" as the specific region to which the antisense oligonucleotide is intended to bind. *See, e.g.*, '851 patent at 4:44–46 ("[T]he invention provides antisense molecules capable of binding to a selected target to induce exon skipping."); *id.* at 23:38–45 ("[T]here is provided antisense molecules capable of binding to a selected target to induce exon skipping."); *id.* at 32:31–36 ("Annealing sites on the human dystrophin pre-mRNA were selected for examination . . . . 2OMe antisense oligonucleotides were

designed to be complementary to the target sequences . . ."). Thus, unlike the other interpretations proffered by NS, a person of ordinary skill in the art would readily understand, with reasonable certainty based on the intrinsic record, that the term "a target region" aligns with this interpretation.[2]

Accordingly, NS has not carried its burden of demonstrating, by clear and convincing evidence, that the term "a target region" is indefinite. In other words, when read in light of the entirety of the Wilton Patents, a person of ordinary skill in the art would be clearly informed, with reasonable certainty, that the term "a target region" has a definite meaning and scope. Thus, the Court, based on the intrinsic record, construes "a target region" to have its plain and ordinary meaning, which is "a segment of the pre-mRNA."

D. "exon 53 of the human dystrophin pre-mRNA"

The claim term "exon 53 of the human dystrophin pre-mRNA" appears in claims 1 and 2 of the '851 patent, claims 1 and 2 of the '590 patent, and claim 1 of the '827 patent. The parties' competing proposed constructions for "exon 53 of the human dystrophin pre-mRNA" are set out in the chart below:

Claim Term	Sarepta's Construction	NS's Construction
"exon 53 of the human dystrophin pre-mRNA"	Not indefinite. **Alternatively:** plain and ordinary meaning, which means "the pre-mRNA transcribed from exon 53 of the human dystrophin gene"	Indefinite

[2] Indeed, Sarepta's own expert, Dr. Michelle L. Hastings, has repeatedly used the term "target region" in her own publications consistent with the disputed term's plain and ordinary meaning. *See, e.g.*, D.I. 171, Ex. 48 at 250 (antisense oligonucleotides "are short oligonucleotides, typically 15–25 bases in length, which are the reverse complement sequence of a specific RNA transcript target region"); *id.*, Ex. 49 at 6550 ("[A]ll [antisense oligonucleotides] make use of short nucleic acids that specifically base-pair to a targeted sequence.").

Like the disputed term "a target region," here the crux of the parties' dispute is whether the term "exon 53 of the human dystrophin pre-mRNA" is indefinite or, whether a person of ordinary skill in the art would understand, with reasonable certainty, its meaning based on the Wilton Patents' intrinsic record. NS contends that "exon 53 of the human dystrophin pre-mRNA" renders the claims indefinite because a person of ordinary skill in the art "would immediately find it unclear whether the claim term 'exon 53 of the human dystrophin pre-mRNA' refers to exon 53 from wildtype pre-mRNA or patient's mutated pre-mRNA." D.I. 166 at 28 (citing D.I. 171, Ex. 43 ¶ 73). Sarepta disagrees, arguing that "[a] skilled artisan would have understood this term to refer to the wild-type sequence of exon 53 of the human dystrophin pre-mRNA" based on the Wilton Patents' intrinsic record. D.I. 166 at 36 (citing D.I. 171, Ex. 53 ¶¶ 35-36).

Applying the same framework as detailed above, *see supra* Section II.C, the Court finds that NS has not met its burden of demonstrating, by clear and convincing evidence, that "exon 53 of the human dystrophin pre-mRNA" is indefinite. *See BASF Corp.*, 875 F.3d at 1365. Neither party disputes that the wild-type sequence of exon 53 of the human dystrophin pre-mRNA is well known in the art. D.I. 171, Ex. 43 ¶ 70 ("[T]he dystrophin gene was identified in the 1980s, and subsequent research has identified the typical nucleotide sequences associated with its various exons, including exon 53."); *id.*, Ex. 37 ¶ 65 ("The dystrophin gene was discovered nearly twenty years before the Wilton patents were filed. . . . The sequence of each exon within the dystrophin gene was well known when the Wilton patents were filed."). Rather, NS contends that, while not dispositive, a person of ordinary skill in the art would also consider, based on the preamble of claim 1 of the '827 patent, that "mutated pre-mRNA" is a reasonable interpretation of the disputed term. D.I. 166 at 28-29; *see* '827 patent at claim 1 ("[A] patient with Duchenne muscular dystrophy (DMD) in need thereof who has a mutation of the DMD gene that is amenable to exon

53 skipping."). However, neither party has offered any evidence that exon 53 is mutated in any DMD patients amenable to treatment by exon 53 skipping. *See* D.I. 171, Ex. 53 ¶ 42. As such, the Court declines to "find indefiniteness based on a hypothetical possibility." *Purdue Pharm. Prods. L.P. v. Actavis Elizabeth L.L.C.*, C.A. No. 12-5311, 2015 WL 5032650, at *57 (D.N.J. Mar. 27, 2015). More so, NS's reliance on the Wilton Patents' specifications discussing experiments conducted with "mutated cell lines," *see, e.g.*, D.I. 166 at 29-30 (citing '851 patent at 3:8-21; *id.* at 3:22-40), is also unpersuasive as these experiments reference a ***different*** exon in a ***non-human*** cell line, which plainly fails to inform the meaning of the term "exon 53 of the human dystrophin pre-mRNA." Thus, finding no support in the intrinsic record, a person of ordinary skill in the art would not consider "mutated pre-mRNA" as a reasonable interpretation of the disputed term. Instead, a person of ordinary skill in the art would understand the term to refer to the wild-type sequence of exon 53 of the human dystrophin pre-mRNA.

This understanding is consistent with the plain language of the claims, which uses the definite article "the" when referring to exon 53 of the human dystrophin pre-mRNA, suggesting that it is referring to "the" sequence known in the art. See *Thorner*, 669 F.3d at 1365 ("The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history.") (internal citation omitted). Notably, too, NS itself has used the term "the 53rd exon in the human dystrophin gene" during the prosecution of its '361 patent to mean the wild-type human pre-mRNA, thereby obviating any purported confusion by NS as to the term's plain and ordinary meaning.

Accordingly, because a person of ordinary skill in the art would understand, with reasonable certainty, the meaning of the disputed term "exon 53 of the human dystrophin pre-

mRNA" based on the Wilton Patents' intrinsic record, "exon 53 of the human dystrophin pre-mRNA" is not indefinite. As NS has not carried its burden of demonstrating, by clear and convincing evidence, that the term is indefinite, the Court construes the disputed term to have its plain and ordinary meaning as commonly understood by a person of ordinary skill in this field—i.e., the "wild-type" human pre-mRNA. *See Phillips*, 415 F.3d at 1316. Thus, the Court, based on the intrinsic record, construes "exon 53 of the human dystrophin pre-mRNA" to mean "the pre-mRNA transcribed from exon 53 of the human dystrophin gene."

E. "the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69)"

The claim term "the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69)" (the "Annealing Site Term") appears in claims 1 and 2 of the '851 patent. The parties' competing proposed constructions for the Annealing Site Term are set out in the chart below:

Claim Term	Sarepta's Construction	NS's Construction
"the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69)"	Not indefinite. **Alternatively**: "the target region is within nucleotides +23 to +69 of exon 53 of the human dystrophin pre-mRNA"	Indefinite

The parties dispute whether the Annealing Site Term renders the claims of the '851 patent indefinite. NS contends that, while the claim language is "easily understood" to require a target region of, at most, nine nucleotides long (from +39 to +47), the Annealing Site Term is indefinite because it is impossible for an "antisense oligonucleotide . . . comprising a base sequence [of] at least 12 consecutive bases" to be "100% complementary to consecutive nucleotides" of a "target region" that is only 9 bases long. D.I. 166 at 66-67. Sarepta disagrees, arguing that a person of

ordinary skill in the art, referencing the claim language and the specification, would understand, with reasonable certainty, that the target region of the claimed antisense oligonucleotide is within two annealing sites, "H53A(+23+47)" and "H53A(+39+69)." *Id.* at 64-65.

Applying the same framework as detailed above, *see supra* Section II.C, the Court finds that NS has not met its burden of demonstrating, by clear and convincing evidence, that the Annealing Site Term is indefinite. *See BASF Corp.*, 875 F.3d at 1365. Contrary to NS's contention, the claim language does not "require[] a 'target region' that is both 'within annealing site H53A(+23+47)' and '[within] annealing site H53A(+39+69).'" *See* D.I. 166 at 66 (citing *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 886 (Fed. Cir. 2004)). Rather, the plain language of claims 1 and 2 of the '851 patent makes clear that the claimed target region falls within a portion bookended by the two annealing sites collectively, i.e., nucleotides +23 to +69 of exon 53 of the human dystrophin pre-mRNA. *See* '851 patent at claims 1, 2. That is, the beginning of the target region is marked by one annealing site (H53(+23+47)), while the other end of the target region is marked by the other annealing site (H53A(+39+69)). NS's construction—that only the region from nucleotides +39 to +47 is "within" ***both*** annealing sites—however, improperly imports a second "within" limitation not present in the claim language. NS's argument that the claims use the conjunctive limitation "and" to require both elements separated by "and" to be met is similarly unpersuasive. D.I. 166 at 66. While "and" may indicate that both elements must be met, "in certain contexts, the word 'and' can reasonably be understood to denote alternatives, rather than conjunctive requirements." *See, e.g.*, *Kaufman v. Microsoft Corp.*, 34 F.4th 1360, 1373 (Fed. Cir. 2022); *Ortho-McNeil Pharm., Inc. v. Mylan Lab'ys, Inc.*, 520 F.3d 1358, 1361-63 (Fed. Cir. 2008) (construing "and" to connote alternatives when construing "and" to have a conjunctive meaning would lead to "nonsensical" results). Here, accepting NS's proposed construction would

create a target region that is "only 9 bases long," i.e., from positions +39 to +47. D.I. 166 at 66-67. Yet, even as NS admits, this construction would render the claims "impossible" because the claims require that the target region is ***at least 12 nucleotides in length*** that are 100% complementary to consecutive nucleotides. *See Ruckus Wireless, Inc. v. Innovative Wireless Sols., L.L.C.*, 824 F.3d 999, 1004 (Fed. Cir. 2016) (a claim should be construed to "preserve its validity" when a reasonable construction is available). Accordingly, NS has not demonstrated, by clear and convincing evidence, that the Annealing Site Term would be understood by a person of ordinary skill in the art to mean only the region from nucleotides +39 to +47, i.e., that is "within" both annealing sites.

In contrast, Sarepta's proposed construction identifies a target region that is forty-seven bases long, i.e., from positions +23 to +69, which is consistent with the remaining claim language requiring "at least 12 consecutive bases" of SEQ ID NO: 195. *See Kaufman*, 34 F.4th at 1373. Sarepta's proposed construction is also supported by the '851 patent's intrinsic record. The specification describes how to interpret the claimed annealing sites, *see* '851 patent at 22:41-65, explaining that a "target region" is expressed in the format of "H#A/D(x:y)"—wherein "H" designates the species, "#" designates the target dystrophin exon, "A/D" identifies the beginning (the 5'-end) or the end (the 3'-end) of the exon, and "(x:y)" represents the annealing coordinates. *Id.* The specification also incorporates a nomenclature system reported in the prior art, which uses four identifiers to define the region of the pre-mRNA targeted by an antisense oligonucleotide: Letter / Number / A or D / Coordinates. D.I. 166 at 63-64 (citing D.I. 171, Ex. 37 ¶¶ 86-87); *see also* D.I. 171, Ex. 37 ¶41. Based on these teachings, a person skill in the art would understand that the claimed annealing sites "H53A(+23+47)" and "H53A(+39+69)" corresponds to nucleotides +23 to +47 ("(23+47)") and nucleotides +39 to +69 ("(+39+69)"), respectively, each counted from

the beginning ("A") of exon 53 ("53") of the human dystrophin pre-mRNA ("H"). Furthermore, a person skilled in the art would also understand that the claimed target region falls within these overlapping annealing sites collectively, i.e., nucleotides +23 to +69 of exon 53 of the human dystrophin pre-mRNA—the beginning marked by one annealing site, i.e., H53(+23+47), and the end marked by the other annealing site, i.e., H53A(+39+69).

To be sure, this construction is also supported by the prosecution history of the '851 patent. *Fenner Invs., Ltd. v. Cellco P'ship*, 778 F.3d 1320, 1323 (Fed. Cir. 2015) ("Any explanation, elaboration, or qualification presented by the inventor during patent examination is relevant" to claim construction). During prosecution of the '851 patent, the applicant faced an obviousness rejection over prior art references disclosing certain antisense oligonucleotides directed to exon 53 of the human dystrophin pre-mRNA. D.I. 169, Ex. 22 at SRPT-VYDS-0004609. In response, the applicant explained that the cited prior art did not render the claimed invention obvious, including "the exon 53 target region +23 to +69." *Id.* at SRPT-VYDS-0004786. Similarly, during prosecution of the '827 patent, the applicant again explained that the Annealing Site Term "delineates a target region on exon 53 that falls within two overlapping annealing sites and thus provides a target region spanning from, and including, endpoint H53A+23 to, and including, endpoint H53A+69." *See* D.I. 169, Ex. 23 at SRPT-VYDS-0006276-77. Although the '827 patent ultimately issued without the Annealing Site Term, the applicant's interpretation conforms to how

a person skilled in the art would interpret the disputed term based on the intrinsic evidence.[3] *Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1350 (Fed. Cir. 2004) ("[A] patentee's statements during prosecution, whether relied on by the examiner or not, are relevant to claim interpretation."). Additionally, during an opposition to prosecution in Europe,[4] NS interpreted a similar phrase—"hybridizable to an exon 53 target region of the Dystrophin gene designated as annealing site H53A(+23+47), annealing site H53A(+39+69), or both"—as referring to the same +23 to +69 target region. D.I. 168, Ex. 11 at 4-5; *see Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1374 (Fed. Cir. 2005). In opposing the prosecution, NS interpreted "both" as referring to "the area from nucleotide +23 until +69," which corresponds to the same region that a person of skill in the art would have identified from reading the Annealing Site Term of the '851 patent. D.I. 168, Ex. 11 at 4-5.

Therefore, when read in light of the entirety of the '851 patent, a person of ordinary skill in the art would be clearly informed, with reasonable certainty, that the Annealing Site Term refers to the region within these overlapping annealing sites collectively, i.e., nucleotides +23 to +69 of exon 53 of the human dystrophin pre-mRNA. NS has not carried its burden of demonstrating, by

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[3] NS agues that, during prosecution of U.S. Reissue Patent No. 47,691 ("the '691 reissue patent"), the patentee acquiesced to the Examiner's indefiniteness rejections by deleting the Annealing Site Term, which purportedly supports NS's indefiniteness contention. D.I. 166 at 67-68. That the applicant ultimately deleted the Annealing Site Term from the '691 reissue patent, however, does "not provide a sufficient reason to adopt a different construction from the one clearly indicated by the rest of the prosecution history." *Univ. of Mass. v. L'Oréal S.A.*, 36 F.4th 1374, 1384 (Fed. Cir. 2022). Indeed, as demonstrated by the remainder of the prosecution history, the applicant repeatedly explained that the phrase covered nucleotides +23 to +69 of exon 53. *See, e.g.*, D.I. 171, Ex. 45 at 29-30 ("spanning from H53A+23 to H53A+69"); *id.*, Ex. 22 at SRPT-VYDS-0004786 ("the exon 53 target region +23 to +69"); D.I. 169, Ex. 23 at SRPT-VYDS-0006277 ("spanning from, and including, endpoint H53A+23 to, and including endpoint H53A+69").

[4] NS opposed the prosecution of European Patent No. 2,206,781 B1, which stemmed from the same original patent application that led to the Wilton Patents. *See* D.I. 171, Ex. 37 ¶¶ 90-91; D.I. 168, Ex. 10.

clear and convincing evidence, that the Annealing Site Term is indefinite. Accordingly, the Court, based on the intrinsic record, construes the Annealing Site Term to mean "the target region is within nucleotides +23 to +69 of exon 53 of the human dystrophin pre-mRNA."

F. "in which uracil bases are thymine bases"

The claim term "in which uracil bases are thymine bases" appears in claims 1 and 2 of the '851 patent, claims 1 and 2 of the '590 patent, and claim 1 of the '827 patent. The parties' competing proposed constructions for the term "in which uracil bases are thymine bases" are set out in the chart below:

Claim Term	Sarepta's Construction	NS's Construction
"in which uracil bases are thymine bases"	Not indefinite. **Alternatively**: plain and ordinary meaning, which means "the antisense oligonucleotide has thymine bases instead of uracil bases"	Indefinite

Once again, the parties' dispute centers around whether the term "in which uracil bases are thymine bases" is indefinite or, whether a person of ordinary skill in the art would understand, with reasonable certainty, its meaning based on the Wilton Patents' intrinsic record. NS contends that the disputed term is indefinite because the antecedent basis for this limitation is not expressly stated, leading to "at least two equally likely interpretations" without guidance to resolve this uncertainty: (1) "the phrase modifies the term 'antisense oligonucleotide' as a whole, such that no uracil bases are included anywhere in the 'antisense oligonucleotide;'" or, (2) "the phrase modifies the sequence of bases immediately preceding it (e.g., SEQ ID NO: 195), such that the at least 12 consecutive bases of SEQ ID NO: 195 includes thymine bases in place of uracil bases." D.I. 166 at 47-48. Sarepta argues that the disputed term is not indefinite because, "[g]uided by the claim

language, specification, and prosecution history, a skilled artisan would have understood that the claimed antisense oligonucleotide includes thymine bases, not uracil bases." *Id.* at 46.

Applying the same framework as detailed above, *see supra* Section II.C, the Court finds that NS has not met its burden of demonstrating, by clear and convincing evidence, that the "in which uracil bases are thymine bases" term is indefinite. *See BASF Corp.*, 875 F.3d at 1365. Starting with the claim language, claim 1 of the '590 patent, which is instructive, recites:

> 1. An antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), ***in which uracil bases are thymine bases***, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping; or a pharmaceutically acceptable salt thereof.

See '590 patent at claim 1 (emphasis added).

The plain language of the claim uses commas to set off each "wherein" and "in which" clause, suggesting that the "in which uracil bases are thymine bases" term modifies the antecedent subject "an antisense oligonucleotide." To be sure, the claim also uses serial commas before every "wherein" and "in which" clause, which generally suggest, as a matter of grammar, a listing of individual, independent items in a series. *See Credle v. Bond*, 25 F.3d 1566, 1572 (Fed. Cir. 1994) ("In determining the true meaning of the language of the count, the grammatical structure and syntax thereof may be instructive. . . . [B]efore each clause . . . there is there is a comma, indicating the beginning of a new, distinct step to be taken in the method of producing the collapsible bags."); *see also* Chicago Manual of Style § 6.19 (17th ed. 2017) (explaining serial commas). Moreover, if the "in which uracil bases are thymine bases" term modified the sequence of bases immediately preceding it, i.e., SEQ ID NO: 195, as NS contends, then there would be no reason the patentee used a comma to separate the "in which uracil bases are thymine bases" term from the rest of the

claim language. *See Becton, Dickinson and Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249, 1257 (Fed. Cir. 2010) ("Claims must be interpreted with an eye toward giving effect to all terms in the claim.") (internal quotation marks omitted). Thus, reading the disputed term in the context of the entire claim language, the syntax and grammar of the claim suggests that the "in which uracil bases are thymine bases" term modifies the antecedent subject "an antisense oligonucleotide." *See Finisar Corp. v. DirecTV Grp., Inc.*, 523 F.3d 1323, 1336 (Fed. Cir. 2008) ("[W]hen a modifier is set off from a series of antecedents by a comma, the modifier should be read to apply to each of those antecedents.").

The intrinsic record of the Wilton Patents further supports this understanding. Looking to the specification, neither party disputes that none of the embodiments use mixtures of uracils and thymines for the antisense oligonucleotides. *See* '851 patent at Table 1A; *see also* D.I. 166 at 51-52 ("As Sarepta correctly notes, the examples in the [Wilton] Patents list oligonucleotides with only uracil bases—not a mixture."). The specifications further explain that thymine bases may be substituted for uracil bases when making a morpholino but are silent as to a combination of both uracil and thymine bases. *See id.*; *see also* '590 patent at Table 1A; '827 patent at Table 1A. Contrary to NS's contention, the prosecution history identified by Sarepta also informs a person of ordinary skill in the art, with reasonable certainty, as to scope of the claims. In overcoming an obviousness rejection to structurally identical claims, the applicant identified "uracil bases [being] thymine bases" as a feature of the claimed antisense oligonucleotide rather than a feature of the preceding "base sequence" limitation. *See* D.I. 169, Ex. 20 at SRPT-VYDS-0094179 ("[T]he pending claims are drawn to an antisense oligonucleotide having the following elements: . . . (ii) 20 consecutive bases of SEQ ID NO: 193; (iii) uracil bases are thymine bases . . ."); *id.* at SRPV-VYDS-0094181 ("[A]n antisense oligonucleotide . . . wherein uracil bases are thymine bases").

The prosecution history also demonstrates that the Examiner understood that the disputed term was intended to modify the entire antisense oligonucleotide, not just the preceding base sequence limitation. *Id.* at SRPT-VYDS0094154-55 (Examiner stating the claims are drawn to "an antisense oligonucleotide . . . wherein uracil bases are thymine bases"). More importantly, the applicant labeled the listed elements of the claim using sequential roman numerals and illustrated the distinct nature of each listed element using the phrase "and wherein."

> Specifically, ***the pending claims*** are drawn to an antisense oligonucleotide having the following elements: ***(i)*** 25 bases comprising a base sequence that is 100% complementary to 25 consecutive bases of exon 53 of the human dystrophin pre-mRNA; ***(ii)*** 20 consecutive bases of SEQ ID NO: 193; ***(iii)*** uracil bases are thymine bases; ***(iv)*** the antisense oligonucleotide is a morpholine; ***(v)*** the antisense oligonucleotide induces exon 53 skipping; ***and (vi)*** the antisense oligonucleotide is chemically linked to a polyethylene glycol chain.

See D.I. 169, Ex. 20 at SRPT-VYDS-0094179 (emphases added).

> Further, none of the cited references teach or suggest combining the elements to result ***in the claimed antisense oligonucleotide***. Specifically, there is no teaching or suggestion to generate an antisense oligonucleotide of 25 bases, ***wherein*** the antisense oligonucleotide comprises 20 consecutive bases of SEQ ID NO: 193, ***and wherein*** uracil bases are thymine bases, ***and wherein*** the antisense oligonucleotide is a morpholino, ***and wherein*** the result antisense oligonucleotide induce exon 53 skipping of the human dystrophin pre-mRNA.

Id. at SRPV-VYDS-0094181 (emphases added).

The applicant's treatment of these claim elements underscores that each listed element, including "uracil bases are thymine bases," independently modifies the antecedent subject "an antisense oligonucleotide" as a whole rather than a feature of the preceding "base sequence" limitation.

Accordingly, when read in light of the entirety of the Wilton Patents' intrinsic record, a person of ordinary skill in the art would be clearly informed, with reasonable certainty, that the term "in which uracil bases are thymine bases" refers to the entire antisense oligonucleotide. NS has not carried its burden of demonstrating, by clear and convincing evidence, that the term is

indefinite. Accordingly, the Court, based on the intrinsic record, construes "in which uracil bases are thymine bases" to mean "the antisense oligonucleotide has thymine bases instead of uracil bases."

III. DISPUTED TERMS – THE NS PATENTS

A. "antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57"

The claim term "antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57" appears in claim 1 of the '361 patent. The parties' competing proposed constructions for "antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57" are set out in the chart below:

Claim Term	NS's Construction	Sarepta's Construction
"antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57"	Plain and ordinary meaning, which means "antisense oligomer with a nucleotide sequence that is the specific nucleotide sequence of SEQ ID NO: 57 (guugccuccg guucugaagg uguuc)"	Plain and ordinary meaning, which means "antisense oligomer having the sequence of SEQ ID NO: 57 (guugccuccg guucugaagg uguuc) with no nucleobase additions, substitutions or modifications thereof.

The parties agree that the term "antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57" should be construed to have its plain and ordinary meaning—that the claimed antisense oligomer has the exact bases "guugccuccg guucugaagg uguuc," i.e., SEQ ID NO: 57. *See* D.I. 173 at 11. Thus, the remaining dispute centers around whether the term "antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57" excludes nucleobase additions, substitutions, and/or modifications. *Id.*

Starting with the claim language, claim 1 of the '361 patent recites:

> 1. An antisense oligomer which causes skipping of the 53rd exon in the human dystrophin gene, consisting of the nucleotide sequence of SEQ ID NO: 57, wherein the antisense oligomer is an oligonucleotide in which the sugar moiety and/or the

> phosphate-binding region of at least one nucleotide constituting the oligonucleotide is modified, or a morpholino oligomer.

See '361 patent at claim 1.

Here, the claim uses the phrase "consisting of," which "is a term of patent convention meaning that the claimed invention contains only what is expressly set forth in the claim," and "excludes any elements, steps, or ingredients not specified in the claim." *Multilayer Stretch Cling Film Holdings, Inc. v. Berry Plastics Corp.*, 831 F.3d 1350, 1358-59 (Fed. Cir. 2016) (quoting *Norian Corp. v. Stryker Corp.*, 363 F.3d 1321, 1331 (Fed. Cir. 2004)). This differs from the transitional phrase "having," which, similar to the transitional phrase "comprising," "can . . . make a claim open." *Crystal Semiconductor Corp. v. Tritech Microelectronics Int'l, Inc.*, 246 F.3d 1336, 1348 (Fed. Cir. 2001). As such, the plain language of the claim 1 of the '361 patent clearly requires that the antisense oligomer has a nucleotide sequence that is reflected in SEQ ID NO: 57, i.e., "guugccuccg guucugaagg uguuc."

Additionally, and contrary to Sarepta's position, there is no intrinsic support for construing the disputed term to ***explicitly*** exclude nucleobase additions, substitutions, and/or modifications thereof. *See Novartis Pharm. Corp. v. Par Pharm. Inc.*, C.A. No. 14-1494-RGA, 2015 WL 7566615, at *4 (D. Del. Nov. 23, 2015) ("Negative limitations will generally not be added to claim terms without 'express disclaimer or independent lexicography in the intrinsic record that justifies including the negative limitation.'" (quoting *Vehicle IP, LLC v. AT&T Mobility, LLC*, 594 F. App'x 636, 642 (Fed. Cir. 2014))). Not only does the transitional phrase "consisting of" already limit the literal scope of the claim to exclude any unrecited elements, *see Multilayer*, 931 F.3d at 1358, but courts have cautioned "that negative limitations, which define an invention in terms of what it does not do rather than what it does, are generally disfavored." *Precision Energy Servs. v. Thrubit, LLC*, 2013 WL 1155250, at *4 (S.D. Tex. Mar. 19, 2013) (citing *Omega Eng'g, Inc. v.*

Raytek Corp., 334 F.3d 1314, 1323 (Fed. Cir. 2003)); *see also Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1349 (Fed. Cir. 2003) ("Rather than insert an additional limitation into the claim, the better course is to rely on a construction . . . that does not require such an interpolation."). Although Sarepta asserts that its negative limitation "simply explains in plain language what the claim excludes,"[5] *see* D.I. 173 at 17, nothing in the specification or prosecution history of the '361 patent suggests that sequences with nucleobase additions, substitutions and/or modifications of SEQ ID NO: 57 must be ***explicitly*** excluded. *See Novartis*, 2015 WL 7566615, at *4.

Accordingly, finding no intrinsic support that justifies including the proposed negative limitation, the Court declines Sarepta's invitation to construe the term to require "no nucleobase additions, substitutions, or modifications thereof." Rather, as informed by the plain language of claim 1 of the '361 patent—i.e., "consisting of"—and supported by the intrinsic record, the Court will construe the disputed term "antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57" to have its plain and ordinary meaning, which is the default in claim construction. *Phillips*, 415 F.3d at 1316. Thus, the Court construes "antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57" to mean "antisense oligomer with a nucleotide sequence that is the specific nucleotide sequence of SEQ ID NO: 57 (guugccuccg guucugaagg uguuc)."

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[5] The cases Sarepta cites in support of including its proposed negative limitation are readily distinguishable. These cases involved disputes over what the plain language of the claim explicitly "excluded." *See* D.I. 173 at 15-16 (citing *Multilayer*, 831 F.3d at 1355-61; *Norian*, 363 F.3d at 1331-32; *Otsuka Pharms. Co. v. Lupin Ltd.*, C.A. No. 21-900-RGA, 2022 WL 2952759, at *3-5 (D. Del. July 26, 2022); *Unimed Pharms., LLC v. Perrigo Co.*, C.A. No. 13-236-RGA, 2015 WL 1094601, at *5-6 (D. Del. Mar. 11, 2015)). Here, however, because the claim language uses the phrase "consisting of," there is no dispute that the literal scope of claim 1 of the '361 patent would exclude any broader disclosures from the specification, such as nucleobase additions, substitutions, or modifications thereof. *See General Elec. Co. v. Int'l Trade Comm'n*, 685 F.3d 1034, 1041 (Fed. Cir. 2012) ("[A] possibly broader disclosure accompanied by an explicit narrow claim shows the inventor's selection of the narrow claim scope.").

B. "e) reacting said Compound 3 with a deprotecting agent to form Compound 4" and "f) reacting [said] Compound 4 with an acid to form said oligomer [or PMO]"[6]

The claim term "e) reacting said Compound 3 with a deprotecting agent to form Compound 4" appears in claims 1 and 6 of the '322 patent, while the claim term "f) reacting [said] Compound 4 with an acid to form said oligomer [or PMO]" appears in claims 1 and 6 of the '322 patent (collectively, the "Reaction Terms"). The parties' competing proposed constructions for the Reaction Terms are set out in the chart below:

Claim Term	NS's Construction	Sarepta's Construction
"e) reacting said Compound 3 with a deprotecting agent to form Compound 4"	Plain and ordinary meaning, which means "chemically reacting Compound 3 with a deprotecting agent, in order to form Compound 4"	Plain and ordinary meaning, which means "chemically reacting a deprotecting agent directly with Compound 3 of step d), which results in Compound 4."
"f) reacting [said] Compound 4 with an acid to form said oligomer [or PMO]"	Plain and ordinary meaning, which means "chemically reacting Compound 4 with an acid, in order to form the oligomer [or the PMO]"	Plain and ordinary meaning, which means "chemically reacting an acid directly with Compound 4 of step e), which results in the oligomer or the PMO. Step f) must occur after step e)."

The parties agree that Reaction Terms require "chemically reacting" at least two ingredients—i.e., Compound 3 and a deprotecting agent, or Compound 4 and an acid—in order to form a specific result—i.e., Compound 4, oligomer, or PMO. D.I. 173 at 29, 52. Thus, the crux of the parties' dispute is two-fold: first, whether the Reaction Terms require a "direct" chemical reaction; and second, whether the Reaction Terms mandate a specific order of steps.

The use of the Reaction Terms in claim 1 of the '322 patent is instructive.

[6] Because of the similarities in parties' arguments related to the Reaction Terms, coupled with the fact that the parties argued the Reaction Terms collectively at the *Markman* hearing, the Court will evaluate these terms together for the purpose of claim construction.

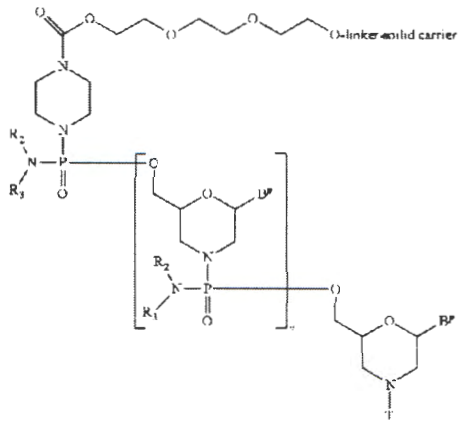
1. A solid-phase method of making an oligomer . . .

said method comprising:

. . .

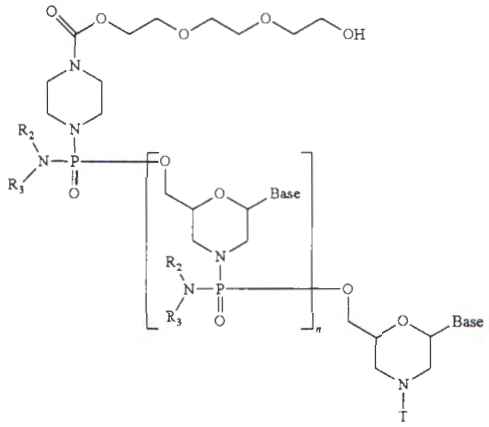
d) repeating steps b) and c) until Compound 3 is complete;

[Compound 3]



e) reacting said Compound 3 with a deprotecting agent to form Compound 4; and

[Compound 4]



f) reacting Compound 4 with an acid to form said oligomer.

See '322 patent at claim 1; *see also id.* at claim 6.

Sarepta contends that a person skilled in the art would readily understand that the plain language of claims 1 and 6 of the '322 patent mandate that the deprotecting agent or acid react directly with Compound 3 or Compound 4, respectively, as opposed to reacting with unrecited

chemical compounds or reagents in an indirect manner. D.I. 173 at 38-39 (citing D.I. 174, Ex. 14 ¶¶ 60-64). However, Sarepta's construction improperly renders the open-ended transitional phrase "comprising" meaningless. *See Wasica Fin.*, 853 F.3d at 1288 n.10 ("It is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous."). As explained above, *see supra* Section II.B, use of the term "'comprising' creates a presumption that the recited elements are only a part of the [invention], that the claim does not exclude additional, unrecited elements." *Multilayer Stretch*, 831 F.3d at 1358 (quoting *Crystal Semiconductor*, 246 F.3d at 1348). A person of ordinary skill in the art, reading the plain language of the claims, would therefore understand that the claimed method does not exclude additional, unrecited reagents, ingredients, or other indirect reactions. *See* D.I. 174, Ex. 15 ¶ 49 ("A [person of ordinary skill in the art] would have understood that as long as the reaction described in Term 2 included both Compound 3 and a deprotecting agent—any number of additional (chemically reactive) reagents could be included in step e)."); *see also id.* at ¶ 71 ("A [person of ordinary skill in the art] would have understood that as long as the reaction described in Term 3 included both Compound 4 and an acid–any number of additional (chemically reactive) reagents could be included."). This understanding is consistent with the specification of the '322 patent, which identifies additional ingredients as being permissibly used along with the deprotecting agent in "step e)" in the same reaction. *See* '322 patent at 22:5-59 ("The 'deprotecting agent' used in this step may also be used as a dilution with, e.g., water, methanol, ethanol, isopropyl alcohol, acetonitrile, tetrahydrofuran, DMF, ..."). The '322 patent's specification further confirms that the reaction need not be "direct" because the result of reacting Compound 4 of step f) with an acid may be an intermediate compound containing H_2+ in place of the trityl group of Compound 4, so an ancillary neutralization step may be required to obtain the final oligomer or PMO. *See id.* at 23:57-67 ("PMO (I) can be

obtained by subjecting the reaction mixture obtained in this step to conventional means of separation and purification such as extraction, concentration, neutralization, . . . Thus, the desired PMO (I) can be isolated and purified.").

While Sarepta argues that its construction accounts for the term "comprising" by allowing for some chemical compounds that "may not chemically react but are added to facilitate the reaction (e.g., a solvent for diluting the deprotecting agent)," *see* D.I. 173 at 39, Sarepta once again defies the plain language of the claims in an effort to improperly limit the Reaction Terms to only "direct" reactions. More so, in arguing that "[t]he specification likewise exclusively depicts a direct reaction between Compound 3 and a deprotecting agent," *see id.* at 50 (citing '322 patent at 22:7-67), Sarepta improperly narrows the meaning of the Reaction Terms to a single embodiment. *See Supercell Oy v. GREE, Inc.*, 2021 WL 4452082, at *4 (Fed. Cir. Sept. 29, 2021) (cautioning courts to avoid construing a term "on the basis of a single exemplary embodiment"). Accordingly, a person of ordinary skill in the art would understand, based on the plain language of the claims and supported by the intrinsic record, that the Reaction Terms do not require that the deprotecting agent or acid react directly with Compound 3 or Compound 4.

By the same token, nothing in the '322 patent's intrinsic record requires that the claimed method be performed in a particular order of steps, as Sarepta contends. See D.I. 173 at 33, 55. Generally, "[a]bsent affirmative indication to the contrary, method steps need not be performed in the order in which they are recited." *Cybersettle, Inc. v. Nat'l Arbitration Forum, Inc.*, 243 Fed. App'x 603 (Fed. Cir. 2007); *cf. Mformation Techs., Inc. v. Research in Motion Ltd.*, 764 F.3d 1392, 1398 (Fed. Cir. 2014) ("[A] claim 'requires an ordering of steps when the claim language, as a matter of logic or grammar, requires that the steps be performed in the order written, or the specification directly or implicitly requires' an order of steps."). Here, the claim language uses

the term "comprising," which "in a method claim indicates that the claim is open-ended and allows for additional [unrecited] steps." *Medichem, S.A. v. Rolabo, S.L.*, 353 F.3d 928, 933 (Fed. Cir. 2003) (quoting *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368 (Fed. Cir. 2003)). However, Sarepta contends that this is not dispositive because the '322 patent's use of an antecedent basis to refer to "said Compound[s]" listed in previous steps necessarily entails that the claimed method be performed in a specific order. *See* D.I. 173 at 33-34, 56-57 ("Here, both the claim language and the specification demonstrate that the claimed synthesis method requires that the recited steps must be carried out in the order specified."). But Sarepta's position relies on a misreading of the claim language. To be sure, claim 1 of the '322 patent provides a "step d)" and defines "Compound 3" using a chemical formula. *See* '322 patent at claim 1. Claim 1 then recites "step e)," which refers to "said Compound 3." *See id.* The claim's use of the word "said" simply "refers back to an earlier phrase in the claim, the scope of the term will be the same as the scope of the earlier language." *Takeda Pharm. Co. v. Sandoz, Inc.*, C.A. No. 12-446, 2013 WL 2153673, at *6 (N.D. Cal. May 16, 2013) (citing *Baldwin*, 512 F.3d at 1343). In other words, a person of ordinary skill in the art would recognize that step e) requires reacting "said Compound 3" as previously defined—i.e., Compound 3 having the same chemical structure as shown in the claim—rather than the results of the prior step. Nothing in the claim language requires the exact compound formed by step d) to be reacted in step e), nor does the claim language foreclose additional, unrecited method steps so long as step e) uses Compound 3 having the same chemical structure as was previously defined.[7] *See Lincoln Nat'l Life Ins. Co. v. Transamerica Fin. Life Ins. Co.*, 2007

[7] The same analysis applies to "step f)," i.e., "reacting [said] Compound 4 with an acid to form said oligomer [or PMO]." Similarly, nothing in the claim language requires the exact compound formed by step e) to be reacted in step f), nor does the claim language foreclose additional, unrecited method steps so long as step f) uses Compound 4 having the same chemical structure as was previously defined.

WL 710119, at *13 (N.D. Ind. Mar. 6, 2007) ("Since the claim is not foreclosed to additional steps, the steps themselves are not foreclosed from being carried out in a different order than stated in the claim."); *see also* D.I. 174, Ex. 15 ¶¶ 58-59.

Furthermore, the Court declines to confine the Reaction Terms to being performed in a particular order on the basis of a single exemplary embodiment. Sarepta argues that, because the "***sole*** synthesis scheme described in the specification follows the precise order of steps recited in the claims, listing steps a) through f) sequentially with no inserted or modified steps," *see* D.I. 173 at 36 (citing '322 patent at 14:1-23:56) (emphasis in original), the claimed method steps must mirror this teaching, *see id.* However, "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom*, 755 F.3d at 1372 (internal quotation marks omitted) (quoting *Liebel-Flarsheim*, 358 F.3d at 906). As explained above, nothing in the intrinsic record demonstrates a clear intention to limit the Reaction Terms to being performed sequentially without alteration. Moreover, although Sarepta contends its "construction allows additional steps to be performed before step a) (e.g., forming Compound 1 used in step a)) and/or after step f) (e.g., purifying the PMO resulting from step f))," Sarepta improperly picks-and-chooses opportunities to benefit from the open-ended term "comprising" while ignoring the consequences of the patentee's chosen language. *See SuperGuide Corp.*, 358 F.3d at 875 (the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language"). There is also no intrinsic support for requiring that "step f)" must occur after "step e)," as Sarepta asserts, *see* D.I. 173 at 57, because a person of ordinary skill in the art would understand that the order of steps e) and f) is not relevant to the claimed method. *See* D.I. 174, Ex. 15 ¶¶ 80-81 (explaining that steps e) and

f) are "polishing" or "finishing" steps and can be performed in any order because they are dependent on the purification methods available to a person of ordinary skill in the art).

Accordingly, as informed by the plain language of claims 1 and 6 of the '322 patent and supported by the intrinsic record, the Court will construe the Reaction Terms to have their plain and ordinary meaning, which is the default in claim construction. *Phillips*, 415 F.3d at 1316. Nothing in the intrinsic record refutes the plain language of the '322 patent's claims, which neither require that the deprotecting agent or acid react directly with Compound 3 or Compound 4, or require that the claimed method be performed in a particular order without the possibility of intermediate reactions. Thus, the Court construes the Reaction Terms to mean "chemically reacting Compound 3 with a deprotecting agent to form Compound 4" and "chemically reacting Compound 4 with an acid to form the oligomer [or the PMO]," respectively.

IV. CONCLUSION

The Court will construe the disputed claim terms as described above. The Court will issue an Order consistent with this Memorandum Opinion.